REMARKS

Claims 5 to 20 remain in the application.

Reconsideration and re-examination of the application on the basis of the claims as amended and the following remarks is respectfully requested.

In the interest of expediating prosecution of the application, applicant has cancelled claims 1 to 4 without prejudice to file a continuation application containing those claims.

Claims 13 to 20 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite. As suggested by the Examiner, claim 13 has amended to delete the preposition "of".

Claims 1 to 4 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite. These claims have been cancelled without prejudice.

With the above amendments it is respectfully submitted that the objection and rejections of the claims under 35 U.S.C. 112 have been overcome.

Claims 1 to 20 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Scheller et al in view of von Borstel et al and Bafundo et al. The Examiner was of the view that the claims in the present invention were *prima facie* obvious in view of combination of Scheller et al, von Borstel et al and Bafundo et al. Applicant respectfully traverses the rejection.

The claims as they presently stand are directed to a method of protecting poultry against coccidiosisa caused by infection by Eimeria which undergoes more than one life cycle. The method comprises administering to the animal a vaccine containing sufficient organisms to develop an immunological response in the animal. The animal is maintained free from chemotherapeutic agents effective against Eimeria for a period of time corresponding to about one life cycle of the organism. Thereafter, the animal is administered a chemotherapeutic agent effective against Eimeria for a period of time corresponding to at

least one life cycle of the infectious organism. As set forth in the present application on pages 10-12, this method permits the animal to be exposed to the entire antigenic compliment of the organism to enable it to develop the full immunological response to the infective organism before the commencement of chemotherapy. The commencing of the chemotherapeutic agent treatment during the second life cycle of the organism allows recycling to occur in the animals such that they are exposed to the organism shed at the end of the first life cycle. The administration of the chemotherapeutic agent limits the effects to the animal from the live vaccine particularly effects evident after the first life cycle of the infectious organism. It is respectfully submitted that the method of the claims and the advantages is not suggested let alone taught by the cited reference either alone or in combination.

Scheller et al teach immunization of rodents with irradiation-attenuated malaria sporozoites to confer preerythrocytic stage-specific immunity to challenge infection. This generation of protective immunity requires delivery of live γ-spz invasion into hepatocytes and γ-spz transformation and further development to exoerythrocytic (EE) stages. The Examiner was of the view that Scheller et al also taught treatment of the immunized rats with primaquine. In fact, while Scheller et al teach immunization to confer protective immunity to malaria, they specifically teach away from the use of primaquine in combination with immunity. Scheller et al used primaquine to demonstrate the role of persistent EErads in conferring protection. They found that treatment with primaquine resulted in the loss of protection conferred by immunization. See last paragraph on page 4067 and data in Table 1.

Von Borstel et al teach the use of acylated derivatives of non-methylated pyrimidine nucleosides capable of attenuating damage to the hematopoietic system in animals receiving antiviral or antineoplastic chemotherapy. Included among the chemotherapeutic agents is 5-fluoroorotate, an analog of the pyrimidine nucleotide precursor orotic acid, which has antiproliferative effects on human cells, but is especially useful for treating infections with malarial parasites, e.g., Plasmodium yoelii or Plasmodium falciparum, which are dependent on de novo pyrimidine biosynthesis. Administration of uridine to mice treated with 5-fluoroorotate attenuated host toxicity due to the latter without impairing its antimalarial activity. However, von Borstel et al provide no teaching of the use of combined vaccination and chemotherapy.

Bafundo et al. teaches a method for protecting an animal against coccidiosis comprising administering to the animal a vaccine, maintaining the animal free of any chemotherapeutic agents for a period beginning with birth or hatching and continuing until sporozoites have penetrated host cells, and thereafter administering a chemotherapeutic agent. The chemotherapeutic agent is administered substantially continuously throughout the life of the animal. Bafundo teaches that the length of delay before administering the chemotherapeutic agent or ionophore should be extremely short, only long enough to permit the coccidia to travel to the relevant section of the intestinal track and invade the host cells. As set forth in the paragraph beginning in column 4, line 45 of Bafundo:

> "the exact number of hours of delay will vary with the identity of the host and the rate of transit through the gastrointestinal tract; and with the particular species of coccidium and the location of the gastrointestinal tract which it infects. In chickens this delay should be on the general order of one to four hours. In cattle, it is expected that the delay be on the order of 4 to 8 hours. It is possible to delay chemotherapeutic treatment for an even longer time period such as up to 24 hours. However, further delay leaves the animal unprotected from coccidiosis, except as has been provided by the immunological process, and is therefore undesirable. The preferred practice, therefore, is to delay ionophore therapy only as long as the time required for sporozoites to penetrate the host cells."

Thus, Bafundo clearly teaches that the commencement of the ionophore or chemotherapeutic agent therapy must start no later than 24 hours after immunization. Delaying beyond this time, the commencement of chemotherapeutic therapy would be going against the teaching of Bafundo.

There is no teaching in the cited art to cause one of skill in the art to ignore the clear teaching of Bafundo et al that the commencment of chemotherapy must be immediate. Scheller et al would clearly teach that, at least with respect to malarial infections, the use of chemotherapy would result in the loss of protection conferred by immunization. Von Borstel et al are completely silent with respect to combined chemotherapy and immunization.

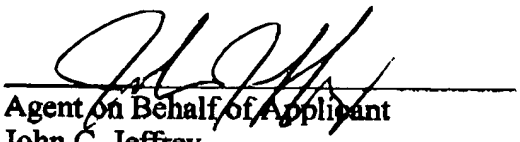
One of skill in the art would have no motivation to combine the teachings of the cited art in the manner suggested by the Examiner. Clearly, Bafundo and Scheller provide opposite teachings, with Bafundo teaching successful use of combined

chemotherapy and immunization and Scheller teaching that chemotherapy results in the loss of protection of immunization. Thus one of skill in the art when developing a therapeutic regime for coccidiosis would look to the teaching of Bafundo and would not be lead to modify Bafundo in any manner by the teaching of Scheller. Von Borstel merely teaches the use of a supplementary therapeutic aid to overcome the side effects of the chemotherapeutic agent for the treatment of malaria. Delaying the administration of the chemotherapeutic agent as set forth in the present claims would be clearly ignoring the teaching of Bafundo that the earliest possible use of the ionophores, no later than 24 hours after immunization, is essential for the practicing of his invention. To delay the introduction of the ionophore or other therapeutic agent beyond 24 hours would require that one go against the teaching of Bafundo to the point of exercising inventive ingenuity as it would have been obvious to one of skill in the art from the teaching of Bafundo that an essential element of his invention is to administer the chemotherapeutic agent within 24 hours.

Accordingly, in view of all the above, it is respectfully submitted that the cited references do not establish that the claims of the present application are obvious, let alone *prima facie* obvious. Rather the proper application of the cited references clearly shows that the present claims define a patentable invention over the art.

In view of all the above, it is respectfully submitted that the application is allowable and early allowance it is hereby requested.

Respectfully submitted



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